

SHITARA, K. et al.
Serial No. 10/009,723
U.S. national phase of PCT/JP00/03957

The attached paper and computer readable copies of the Sequence Listing are the same. No new matter has been added. A separate Statement to this effect is attached.

The specification has been amended to include a new page 77 wherein sequence identifiers have been added. A marked up copy of amended page 77 is also attached wherein the changes are indicated by underlining and strike-out.

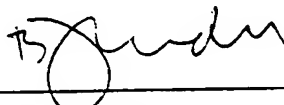
Nothing further is believed to be required in response to the attached Notice however the Examiner is requested to advise the undersigned if otherwise.

An early and favorable Action on the merits is requested.

Respectfully submitted,

NIXON & VANDERHYTE P.C.

By: _____



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Fig. 46 is a graph showing the activity of anti-human VEGF receptor Flt-1 human chimeric antibody KM2550 and human CDR-grafted antibodies KM8550, KM8551, KM8552, KM8553, KM8554 and KM8555 to inhibit the binding between human VEGF and human VEGF receptor Flt-1.

5 Fig. 47 is a graph showing amino acid sequences of the H chain variable regions of anti-human VEGF receptor Flt-1 human chimeric antibody and CDR-grafted antibody. In the drawing, KM1750mouse shows H chain variable region amino acid sequence of KM1750 (SEQ ID NO:93); KM1750HV0 (SEQ ID NO:94) shows an amino acid sequence constituted by inserting CDR of H chain variable region of KM1750 into a human framework; and KM1750HV3 (SEQ ID NO:95) shows an amino acid sequence in
10 in which some of the amino acid sequence of the framework of KM1750HV0 (SEQ ID NO:94) are substituted with the amino acids of KM1750mouse (SEQ ID NO:93).

 Fig. 48 is a graph showing amino acid sequences of L chain variable region of anti-human VEGF receptor Flt-1 human chimeric antibody and CDR-grafted antibody.
15 In the drawing, KM1750mouse (SEQ ID NO:96) shows an amino acid sequence of L chain V region of KM1750 (SEQ ID NO:96); KM1750LV0(I) (SEQ ID NO:97) show an amino acid sequence constituted by inserting CDR of L chain variable region of KM1750 (SEQ ID NO:96) into a human framework; and KM1750LV4 (SEQ ID NO:98) shows an amino acid sequence in which some of the amino acid sequence of the framework of
20 {KM1750LVO(IV) (SEQ ID NO:99)} are substituted with the amino acids of KM1750mouse (SEQ ID NO:96).

Fig. 46 is a graph showing the activity of anti-human VEGF receptor Flt-1 human chimeric antibody KM2550 and human CDR-grafted antibodies KM8550, KM8551, KM8552, KM8553, KM8554 and KM8555 to inhibit the binding between human VEGF and human VEGF receptor Flt-1.

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Fig. 48 is a graph showing amino acid sequences of L chain variable region of anti-human VEGF receptor Flt-1 human chimeric antibody and CDR-grafted antibody.
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20 ~~KM1750LV0(I)~~ { KM1750LVO(IV) (SEQ ID NO:99) } are substituted with the amino acids of KM1750mouse (SEQ ID NO:96).